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ABSTRACT

The research projects during this period were focused on oxidation chemistry involving electron-transfer processes and molecular oxygen. Major accomplishments of our investigations include the following:

(1) The stereochemical course of the DCA-sensitized electron-transfer photo-oxygenation of *cis*- and *trans*-2,3-bis(4-methoxyphenyl) oxirane has been elucidated. The reaction proceeds by a chain reaction to yield exclusively the cis ozonide. An investigation of the photo-isomerization of these epoxides under an inert atmosphere provided additional evidence for a mechanism involving a carbonyl ylide as the key intermediate.

(2) Adamantyl-substituted alkenes were found to undergo oxygenation via non-photochemical process to form stable 1,2-dioxetanes. Treatment of the alkenes with a catalytic amount of tris(p-bromophenyl)ammoniumyl hexachloroantimonate in oxygen-saturated dichloromethane results in high yields of the dioxetanes. Direct oxygen transfer from metal(VI)oxodiperoxo complexes [$(Py)CrO(O_2)_2$ and $(Py)MoO(O_2)_2$] to the alkenes can also be used to prepare these novel peroxides.

(3) A mechanistic study of the S-oxygenation of substituted thioanisoles by horseradish peroxidase and chloroperoxidase has shown that both electron exchange and direct oxygen-atom transfer are involved in these reactions.

COSENSITIZED ELECTRON-TRANSFER PHOTOOXYGENATION

FINAL REPORT

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27 June 1988

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ABSTRACT

The research projects during this period were focused on oxidation chemistry involving electron-transfer processes and molecular oxygen. Major accomplishments of our investigations include the following:

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PUBLICATIONS ACKNOWLEDGING ARO SUPPORT

1. A. P. Schaap, S. Siddiqui, G. Prasad, E. Palomino, and M. Sandison, The Photochemical Preparation of Ozonides by Electron-Transfer Photooxygenation of Epoxides, *Tetrahedron (Symposium-in-Print), 41,* 2229 (1985).

2. S. Kobayoshi, M. Nakano, T. Goto, T. Kimura, and A. P. Schaap, Evidence for the Peroxidase-Dependent Oxygen Transfer from Hydrogen Peroxide to Sulfides, *Biochem. Biophys. Res. Comm., 135,* 166 (1986).

3. S. Kobayashi, M. Nakano, T. Kimura, and A. P. Schaap, The Mechanism of Peroxidase Catalyzed Oxygen Transfer, *Biochem., 26,* 5019 (1987).

4. R. Curci, L. Lopez, L. Troisi, S. M. K. Rashid, and A. P. Schaap, Synthesis of 1,2-Dioxetanes via Electron-Transfer Oxygenation, *Tetrahedron Lett.,* 5319 (1987).

5. M. Chopp, H. Farmer, F. Hetzel, and A. P. Schaap, In-Vivo P-31 NMR Spectroscopy of Mammary Carcinoma Subjected to Subcurative PDT, *Photochem. Photobiol., 46,* 819(1987).

6. R. Curi, L. Lopez, L. Troisi, S. M. K. Rashid, and A. P. Schaap, Oxidation of Enol Ethers by Metal(VI) Oxide Diperoxides, *Tetrahedron Lett.,* in press.

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SUMMARY OF ARO-SUPPORTED RESEARCH

1. Introduction - Mechanisms of Photooxygenation. Two general mechanisms for the oxidation of organic and biological substrates under the influence of light, oxygen, and a sensitizer have been identified (Scheme 1). One process involves the absorption of visible light by a sensitizer (usually a dye) with subsequent energy transfer to ground state oxygen to produce singlet oxygen ($^1O_2$). This metastable species exhibits high reactivity towards a variety of organic substrates including alkenes, dienes, aromatic hydrocarbons, and sulfides.[1] A second type of photosensitized oxygenation results from transfer of an electron or hydrogen atom in a direct interaction of the excited sensitizer and organic substrate. Reaction of the radical intermediates with oxygen yields the oxidation products.

Scheme 1
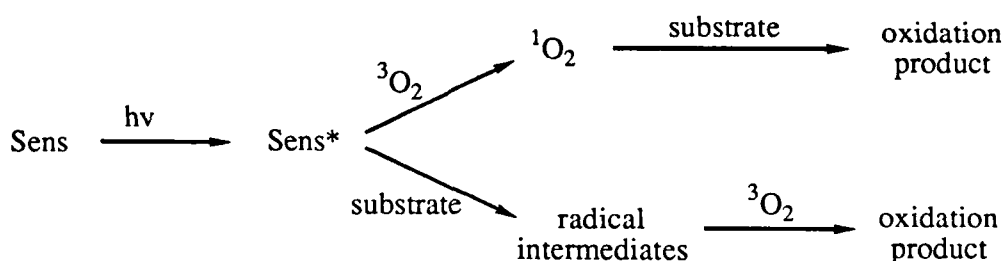
An example of this second type of oxidation process is electron-transfer photooxygenation with cyano-substituted aromatic sensitizers such as 9,10-dicyanoanthracene (DCA). DCA-sensitized oxygenations of alkenes, dienes, acetylenes, and sulfides have been reported.[2] Photooxygenations with DCA are carried out in polar solvents such as acetonitrile using 400 nm light. Quenching of singlet excited DCA by the substrate results in electron transfer and formation of DCA$^-$ and the substrate radical cation. Although this electron-transfer process had been postulated from correlations of quenching rate constants and free energies of electron transfer[3,4] and from solvent-dependent exciplex emissions,[5] the first <u>direct</u> evidence for the photochemical generation of the DCA radical ion was provided by our group.[6,7] The ESR spectrum of this species was observed upon irradiation of solutions of DCA and various quenchers in deoxygenated acetonitrile. The spectrum was identical to that reported by Brunner and Dorr for DCA$^-$ prepared by metal/ammonia
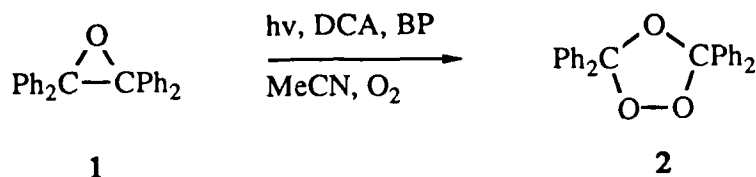
reduction.[8]

The free energy (ΔG) involved in the electron-transfer quenching of $^1DCA^*$ is given by the Weller[3] equation:

$$\Delta G = 23.06 \ [E(S/S^+) - E(DCA^-/DCA) - e^2{}_0/a\varepsilon - \Delta E_{0,0}]$$

where $E(S^+)$ is the oxidation potential of substrate, $E(DCA^-/DCA)$ is the reduction potential of the sensitizer, $e^2{}_0/a\varepsilon$ is the energy gained by bringing the two radical ions to encounter distance a in the solvent of dielectric constant ε ($\cong 0.06$ eV in MeCN), and $\Delta E_{0,0}$ is the electronic excitation energy of DCA. For DCA where $E(DCA^-/DCA) = -0.98$ V vs. SCE in MeCN and $\Delta E_{0,0} = 2.89$ eV, Foote has calculated that electron-transfer quenching of $^1DCA^*$ should be exothermic for substrates with oxidation potentials less than 2 V relative to SCE.[4] Subsequent steps in the mechanism for electron-transfer photooxygenation are: (1) transfer of an electron from DCA^- to oxygen to generate $O_2{}^-$ and (2) reaction of $O_2{}^-$ or $^3O_2$ with S^+ to yield the peroxidic products.
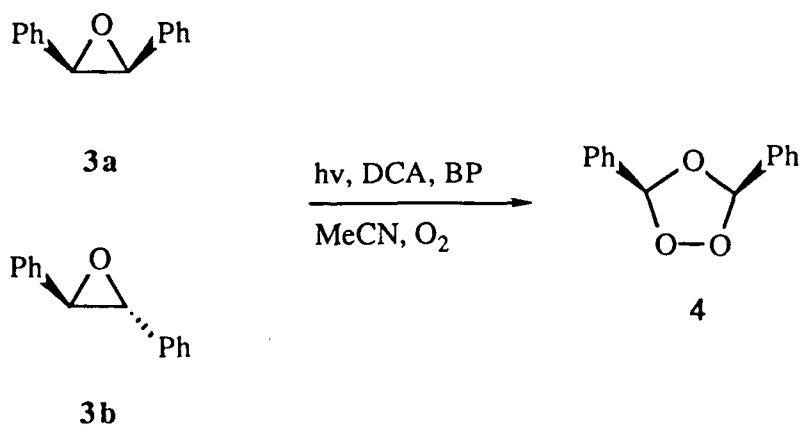
Photooxygenations by the above process are limited to those substrates that quench the fluoresence of DCA. However, a method was developed by our group for the electron-transfer photooxygenation of compounds that have oxidation potentials greater than 2 V and that consequently do not quench singlet excited DCA.[9] For example, epoxides that are unreactive under standard DCA-sensitized conditions can be readily converted to the corresponding ozonides in high yield by use of a non-light-absorbing aromatic hydrocarbon (biphenyl, BP) as a catalyst or cosensitizer in conjunction with DCA.[9-13] Other investigators have subsequently shown that DCA-BP cosensitization can provide dramatically enhanced rates of photooxygenation for a wide variety of substrates.

2. Photochemical Conversion of Epoxides to Ozonides.

Our ARO-supported research on photooxygenation resulted in the first report of the photochemical conversion of an epoxide to an ozonide.[9] The photooxygenation of tetraphenyloxirane (1) was initially carried out in acetonitrile with only DCA as the sensitizer. Although the reaction required over 40 h irradiation with a 450-W Hg lamp, ozonide 2 could be isolated in 51% yield. The slow rate of the reaction was

$$\text{Ph}_2\text{C}\!\!-\!\!\overset{\displaystyle O}{\overset{\diagdown\!\diagup}{}}\!\!\text{CPh}_2 \quad \xrightarrow[\text{MeCN, O}_2]{\text{hv, DCA, BP}} \quad \text{Ph}_2\text{C}\overset{O}{\underset{O\!-\!O}{}}\text{CPh}_2$$

1   **2**

not surprising as **1** exhibits an oxidation potential above 2 V and does not measurably quench the fluorescence of DCA in acetonitrile. We found, however, that a significant enhancement in the rate of the DCA-sensitized photooxygenation of epoxide **1** was observed in the presence of biphenyl (BP). Addition of 1×10^{-2} M BP to the reaction solution resulted in complete conversion of **1** in 10 min and formation of 93% ozonide **2**. Control experiments showed that: (1) no oxidation occurs in the absence of DCA; (2) BP is not consumed in the reaction; (3) ozonide **2** is stable to the photooxygenation conditions and (4) epoxide **1** is not oxidized upon irradiation with a 400-W high-pressure sodium lamp with Rose Bengal in acetonitrile, indicating that **1** does not react with $^1O_2$ directly.

Insight into the mechanism of this reaction was obtained by an investigation of the DCA-BP cosensitized photooxygenation of *cis*-2,3-diphenyloxirane (**3a**) and *trans*-2,3-diphenyloxirane (**3b**).[11] We observed that photooxygenation of **3a** and **3b** gives rise exclusively to the cis ozonide **4**. Authentic samples of *cis*- and *trans*-3,5-diphenyl-1,2,4-trioxolane were obtained from a mixture prepared by ozonation of *trans*-stilbene.

3a

3b

$$\xrightarrow[\text{MeCN, O}_2]{\text{hv, DCA, BP}}$$

4

We have proposed that BP acts as a cosensitizer in photooxygenations by a process analogous to homogeneous redox catalysis for electrode reactions.[10] Epoxides **1** and **3** do not quench the

fluorescence of DCA in MeCN as is expected for compounds with oxidation potentials greater than 2 V vs. SCE (*trans*-2,3-diphenyloxirane (**3b**), $E^{ox}_p = 1.89$ V vs. $Ag/AgNO_3$ in MeCN[14]; ≈ 2.2 V vs. SCE in MeCN). However, BP is more easily oxidized ($E^{ox}_p = 1.90$ V vs. SCE in MeCN) than the epoxides and therefore quenches $^1DCA^*$ more efficiently (k_q for BP = 3.1×10^9 M^{-1} s^{-1}) to generate DCA^- and BP^+. Although energetically unfavorable, a reversible electron transfer from the epoxides to BP^+ could generate the unopened epoxide radical cation. This step would be driven by the subsequent formation of the ring-opened radical cation and irreversible reaction with O_2^- to yield the ozonide.

Of additional interest are the mechanistic implications of the exclusive formation of cis ozonide **4** from both epoxides **3a** and **3b**. These results are not consistent with a mechanism involving attack of O_2^- on epoxide radical cation **5** to give long-lived biradical or zwitterion intermediates. Such mechanisms would predict the formation of a mixture of isomeric ozonides. A plausible mechanism that is consistent with the stereoselective formation of ozonide **4** involves: (1) formation of the most stable E,E-conformation of epoxide radical cation **5** from either **3a** or **3b**; (2) subsequent reduction of **5** by O_2^- (or DCA^-) to yield the E,E-isomer of carbonyl ylide **6**; and (3) addition of oxygen (grounded state or singlet excited) to **6**.

Scheme 2
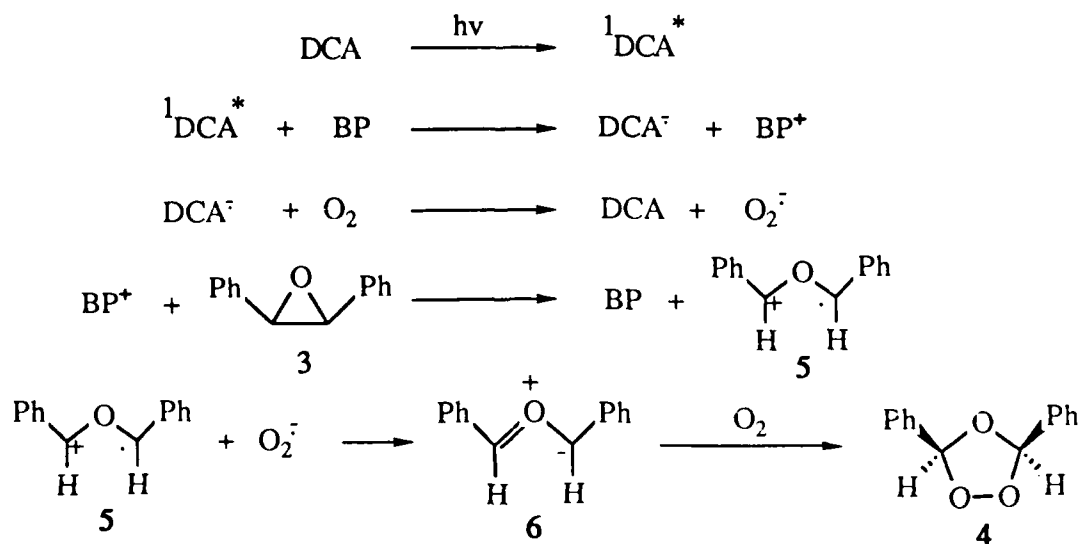
In 1984 Ohta[15] reported that the DCA-sensitized photooxygenation of *trans*-2,3-bis(4-methoxyphenyl)oxirane (**7b**) in the absence of biphenyl resulted in the quantitative formation of a single ozonide which was assigned trans sterochemistry. Our previous investigations had, however, shown that both DCA-sensitized and DCA-biphenyl-cosensitized photooxygenations of dinaphthyl- and diphenyl-substituted epoxides, respectively, lead to exclusive formation of cis ozonides. Therefore, a more complete study of the photooxygenation of **7b** and related epoxides has been carried out in our laboratory.[16]

Epoxides **7a** and **7b** were synthesized from the meso-diol, obtained by LAH reduction of anisoin (Scheme 3). Treatment of the diol with trimethyl orthoacetate, followed by trimethylsilyl chloride, and KOH afforded both **7a** and **7b** in 40% yield. The epoxides were separated by recrystallization and flash chromatography.

Scheme 3

Ar = 4-MeOC$_6$H$_4$-

1) MeC(OMe)$_3$
2) TMSCl
3) KOH

7a   **7b**
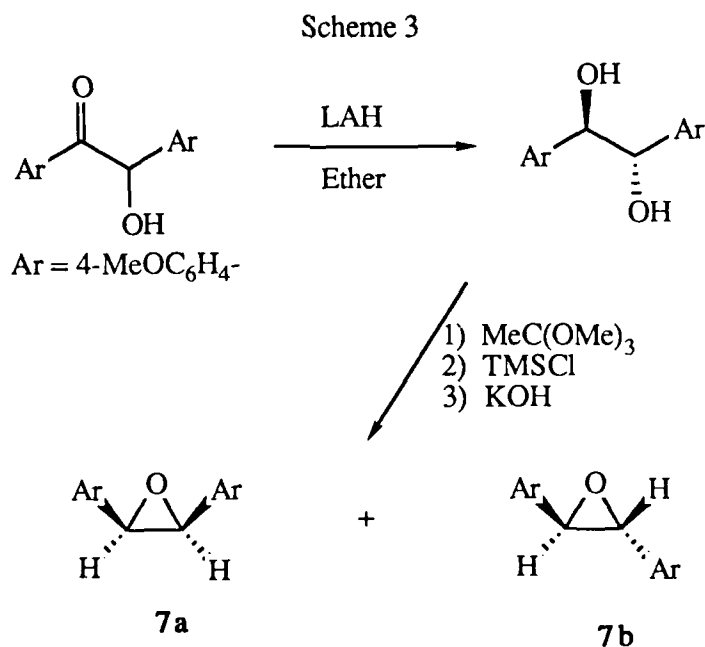
Oxidation potentials for the epoxides were estimated from the irreversible cyclic voltammograms observed in acetonitrile vs. SCE: **7a** (1.27 V) and **7b** (1.24V). Stern-Volmer studies were conducted in acetonitrile under argon and gave rate constants for quenching of the singlet excited state of DCA: **7a** (1.31×10^{10} M^{-1} s^{-1}) and **7b** (1.24×10^{10} M^{-1} s^{-1}).

DCA-sensitized photooxygenations were conducted with a 1000-W high pressure mercury lamp with a CuSO$_4$-filter solution. The progress of the reaction was monitored by reverse-phase HPLC and 300 MHz ^{1}H NMR in CDCl$_3$. Photooxygenation of **7a** and **7b** resulted in the formation of a

single ozonide **8** in 83 and 89% yields, respectively. A small amount of p-anisaldehyde was also formed during the reactions. NMR analysis of the reaction at partial conversion demonstrated that the epoxides are not isomerized under these conditions. Treatment of the ozonide with Ph_3P resulted in conversion to the aldehyde with concomitant formation of Ph_3PO.

7a

hv, DCA

MeCN, O_2

Ar = 4-$MeOC_6H_4$-

7b

8
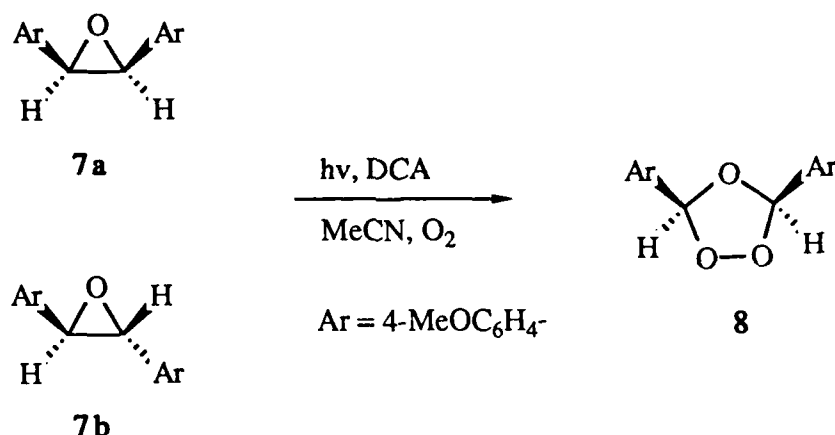
The stereochemistry of the photo-ozonide was established by comparison of ^{1}H NMR chemical shifts of **8** with samples of both isomers of the ozonide (Table 1). A mixture of *cis-* and *trans-* 3,5-diphenyl-1,2,4-trioxolane (40/60) was prepared by ozonolysis of stilbene. The major ozonide had previously been identified as trans by Criegee[17] using chiral chromatography. Ozonolysis of 4,4'-dimethoxystilbene also resulted in a mixture of stereoisomeric ozonides (80/20). On the basis of the NMR chemical shifts in three different solvents, it seems clear that photo-ozonide **8** is cis rather than trans as earlier claimed by Ohta. Thus, the stereochemical course of this photooxygenation is consistent with our earlier observations.

Additional mechanistic information concerning this reaction was provided by the observation that cis epoxide **7a** could be photochemically isomerized to trans **7b** in the presence of DCA under argon. However, irradiation of **7b** under the same conditions did not afford any detectable amount of **7a**.
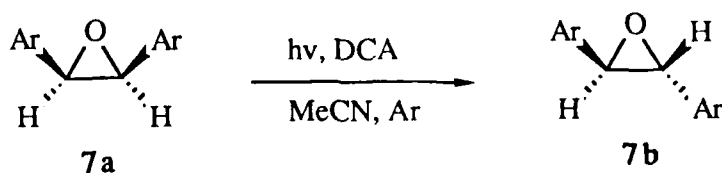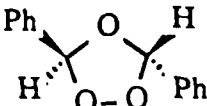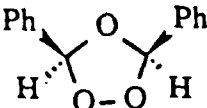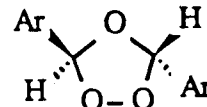

7a

hv, DCA

MeCN, Ar

7b
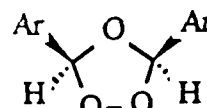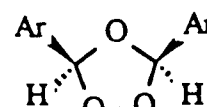
Table 1. Stereochemical Identification of Ozonide **8** by Proton NMR.

| Structure | Source | NMR Solvent | | |
		$CDCl_3$	C_6D_6	CCl_4
Ph–O–H / H–O–O–Ph	major isomer from ozonolysis	6.359	6.256	6.232
Ph–O–Ph / H–O–O–H	minor isomer from ozonolysis	6.329	6.135	6.214
Ar–O–H / H–O–O–Ar	major isomer from ozonolysis	6.319	6.355	6.202
Ar–O–Ar / H–O–O–H	minor isomer from ozonolysis	6.280	6.190	6.138
Ar–O–Ar / H–O–O–H	photo-ozonide **8**	6.280	6.200	6.140

Quantum yields for the photoreactions were determined using Aberchrome 540 as a chemical actinometer.[18] Photooxygenations of **7a** and **7b** with DCA in acetonitrile were carried out to less than 10% conversion. Quantum yields were calculated for five different epoxide concentrations (Tables 2 and 3). Extrapolation of reciprocal plots of Φ vs epoxide concentration gave values for Φ at infinite epoxide concentration (Figures 1 and 2). The quantum yields for **7a** and **7b** are in excess of unity indicating that a chain mechanism is operative in these photooxygenations.

Quantum yields for the photo-isomerization of **7a** to **7b** were similarly determined (Table 4 and Figure 3). Significantly, the limiting quantum yield for the oxygenation and isomerization are the same within experimental error. These results suggest that both processes proceed through common pathways. The following mechanism has been proposed to account for these observations (Scheme 4). Singlet excited DCA is quenched by the electron-rich epoxide **7a** or **7b** with formation of DCA⁻ and the epoxide radical cation. A carbonyl ylide is formed by electron transfer from a second epoxide to the cation in a chain propagating step. In the absence of oxygen, this ylide can be trapped by a dipolarophile such as dimethyl acetylenedicarboxylate or can cyclize to reform th. trans epoxide in an allowed electrocyclic process. In the presence of oxygen, the carbonyl ylide is rapidly converted to the ozonide.
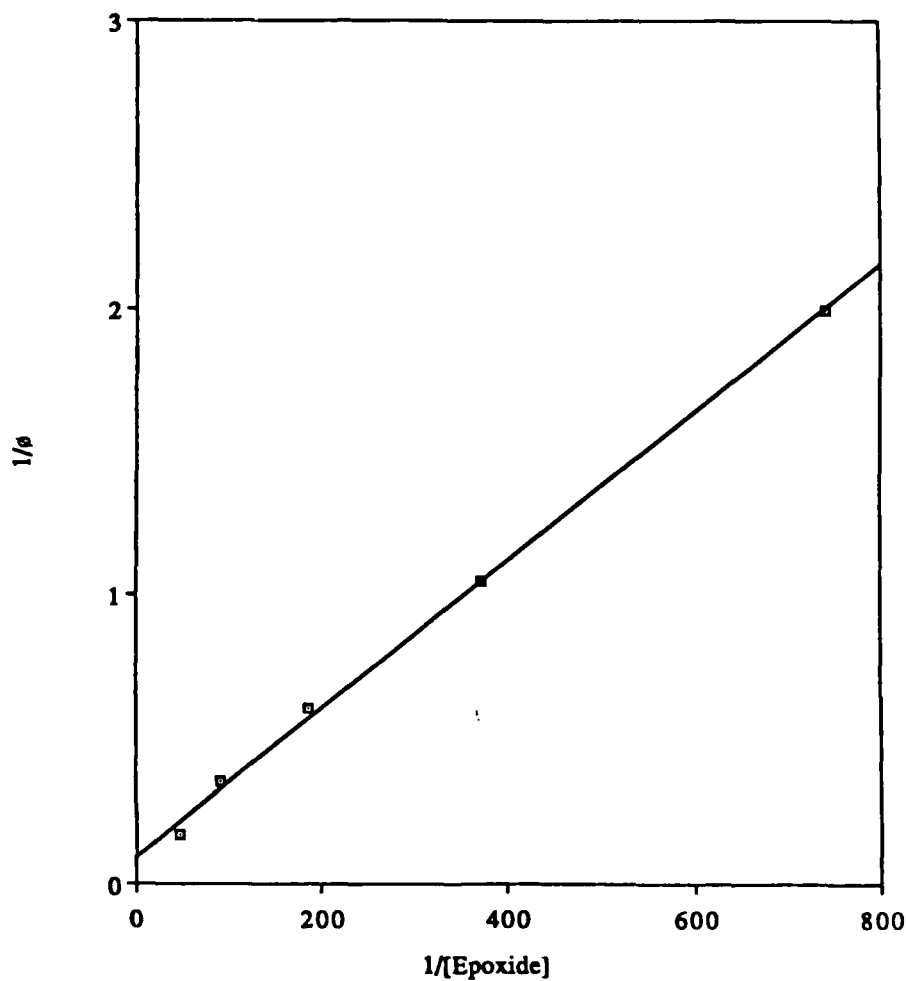
Scheme 4
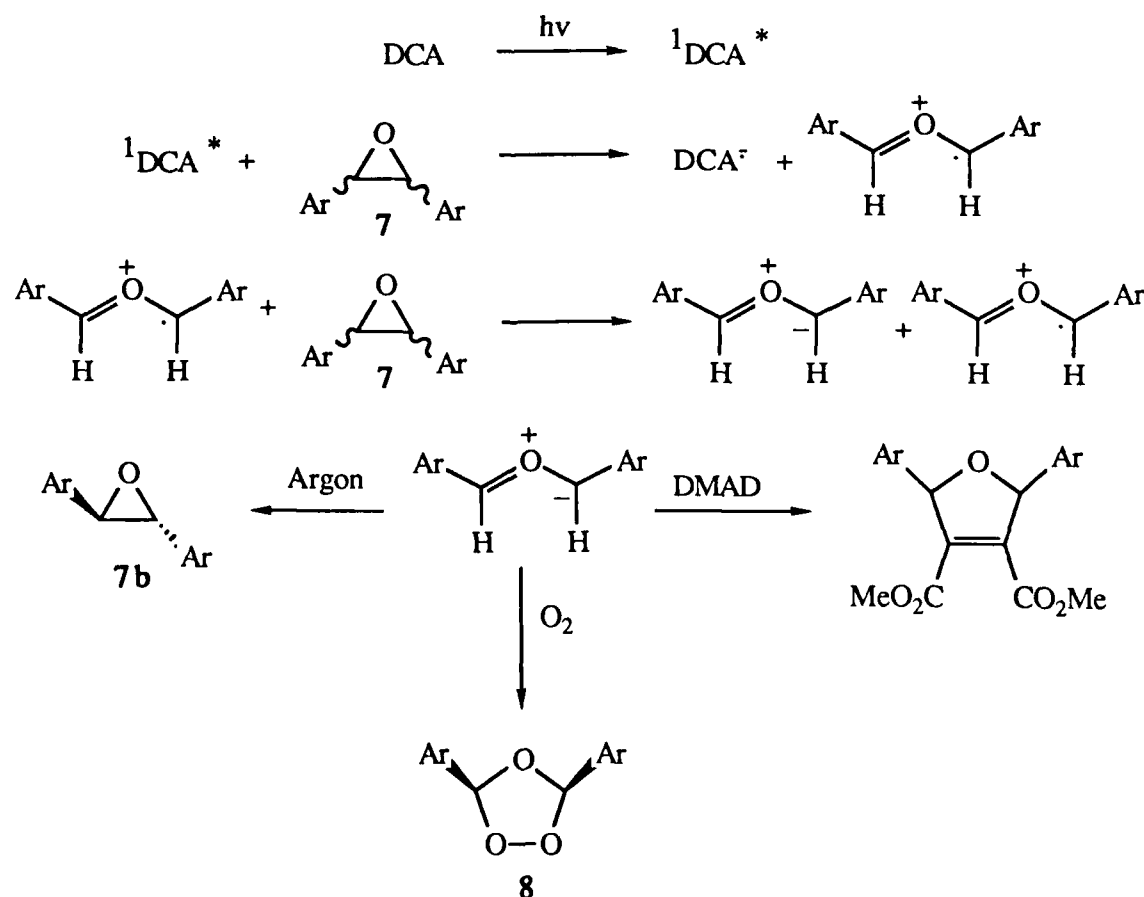
Figure 1. Double reciprocal plot of photooxygenation quantum yield vs. epoxide concentration for **7a** in acetonitrile ($\phi_{lim} = 10.8$, $r = 0.999$).

Table 2. Quantum Yields for the Photooxygenation of **7a**

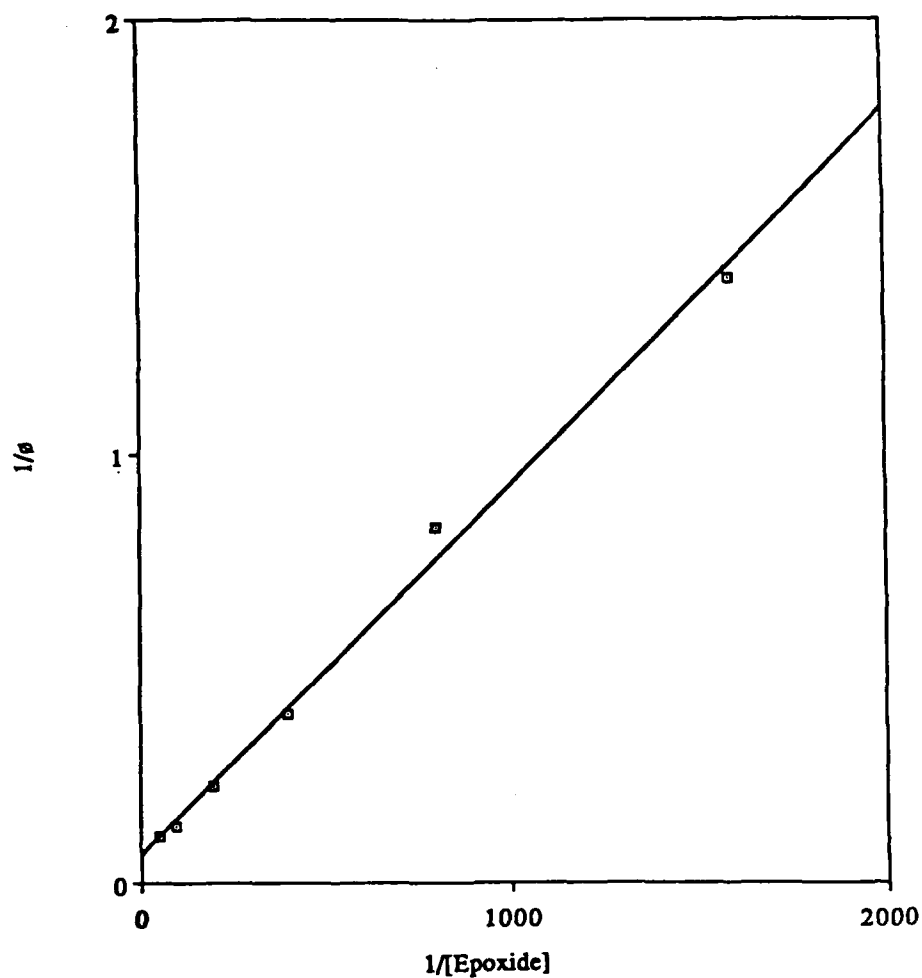| [Epoxide]*	ϕ
2.15×10^{-2}	5.96
1.08×10^{-2}	2.83
5.39×10^{-3}	1.65
2.69×10^{-3}	0.95
1.35×10^{-3}	0.50

*The epoxide concentrations are in mole liter^{-1}.

Figure 2. Double reciprocal plot of photooxygenation quantum yield vs. epoxide concentration for **7b** in acetonitrile ($\phi_{lim} = 15.2$, $r = 0.997$).

Table 3. Quantum Yields for the Photooxygenation of 7b

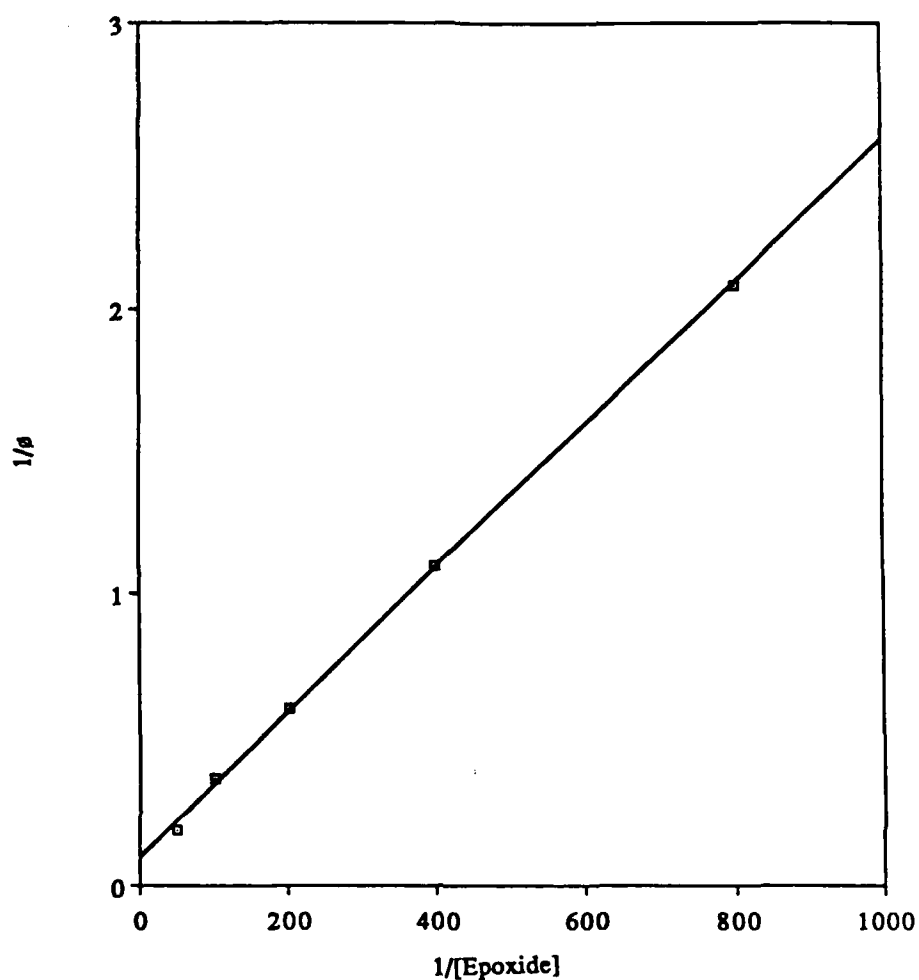| [Epoxide]*	ϕ
2.02×10^{-2}	9.25
1.01×10^{-2}	7.70
5.05×10^{-3}	4.38
2.53×10^{-3}	2.54
1.26×10^{-3}	1.21
6.30×10^{-4}	0.71

*The epoxide concentrations are in mole liter^{-1}.

Figure 3. Double reciprocal plot of photo-isomerization quantum yield vs. epoxide concentration for **7a** in acetonitrile (ϕ_{lim} = 10.8, r = 0.993).

Table 4. Quantum Yields for the Photo-isomerization of **7a**

| [Epoxide]*	ϕ
2.00 x 10^{-2}	5.31
9.98 x 10^{-3}	2.72
4.99 x 10^{-3}	1.64
2.50 x 10^{-3}	0.91
1.25 x 10^{-3}	0.48

*The epoxide concentrations are in mole liter^{-1}.

3. Synthesis of 1,2-Dioxetanes by Electron-Transfer Oxygenation.

In 1980 we reported that 1,2-dioxetanes can be produced by electron-transfer oxidation.[6] DCA-sensitized photooxygenation of diaryl-1,4-dioxenes rapidly gave the corresponding dioxetanes. The dioxetanes could also be produced by a non-photochemical process involving one-electron oxidation of the alkene to its radical cation with tris(p-bromophenyl)ammoniumyl tetrafluoroborate [Ar_3N^+, BF_4^-]. Subsequent reaction of the olefinic radical cation with oxygen afforded the dioxetane. The groups of Nelsen[19], Clennan[20], and Ando[21] have now shown that electrochemical methods can also be used to prepare dioxetanes.

We have recently discovered new methods for controlling the chemiluminescent decomposition of dioxetanes.[22] These processes involve the chemical or enzymatic conversion of a highly stable dioxetane into an unstable form which cleaves spontaneously to generate light. Of particular significance is the application of these novel luminescent compounds to ultrasensitive enzyme-linked immunoassays and DNA probes.

In collaboration with the group of Professor Curci (University of Bari, Italy), we have initiated an investigation of alternative methods for the syntheses of these novel new dioxetanes. High yields of dioxetanes of the general structure **10** can be obtained by electron-transfer oxygenation of the corresponding alkene **9** using a catalytic amount of tris(p-bromophenyl)ammoniumyl hexachloro-antimonate in oxygen-saturated dichloromethane.[23]

4. Oxidation of Enol Ethers by Metals (VI) Oxide Diperoxides.

We have also demonstrated that the metal (VI) oxodiperoxo complexes $(Py)CrO(O_2)_2$ and $(Py)MoO(O_2)_2$ react with alkenes **9** in $CHCl_3$ at 0 °C under an inert atmosphere to yield the corresponding dioxetanes **10**. $^{18}O_2$ labelling studies have demonstrated that the reaction proceeds by oxygen atom transfer from the complex to the alkene with formation of an intermediate epoxide followed by a second oxygen transfer to yield the dioxetane.[24]
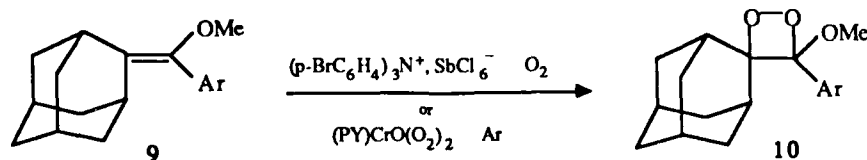
5. Mechanism of Peroxidase-Catalyzed Oxygen-Transfer Reactions.

Peroxidases are heme proteins that catalyze peroxide-dependent oxidations of a wide variety of organic molecules. The catalytic cycle involves two intermediate forms of the enzyme, compounds I and II. The active species are able to effect one electron oxidations of substrates to produce free radicals which undergo coupling, disproportionation, and/or reaction with molecular oxygen.[25]

In collaboration with Profesor Minoru Nakano (Gunma University, Japan), we have recently shown that peroxidases such as horseradish peroxidase (HRP) and chloroperoxidase (CPO) can participate in direct oxygen atom transfer reactions as well as in electron exchange processes.[26] We have investigated the H_2O_2-dependent mono-oxygenation of sulfides to form sulfoxides in the presence of HRP and CPO. Treatment of the substituted thioanisoles 11 with HPO or CPO in acteate buffer (pH 5) in the presence of H_2O_2 gave the corresponding sulfoxides 12 in high yields. Rate constants for the reactions were found to increase in the order of the electron-donating ability of the substituents (Table 5). These results suggest that electron-transfer processes to form the sulfide radical cation as a key intermediate are involved. ^{18}O-labelling studies provided evidence that direct oxygen atom transfer to sulfides also occurs during both HRP- and CPO-catalyzed oxygenations. Stereochemical studies with p-methylthioanisole and CPO showed that the R enantiomer of the sulfoxide is formed with 12.7% ee. No induction of optical activity was observed with HRP.
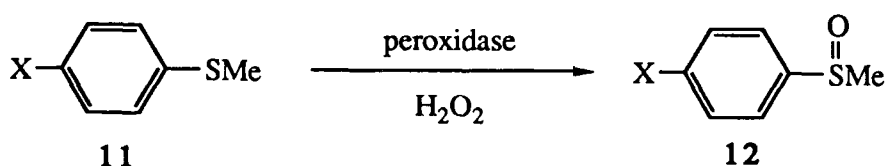

Table 5. Rate Constants for HRP- and CPO-Dependent S-Oxygenation of Substituted $p\text{-}X\text{-}C_6H_4\text{-}S\text{-}Me$ $k_{cat} \times 10^{-5}M^{-1}s^{-1}$

Substituent (X)	HRP	CPO
Me_2CHO-	35.5	3.97
$MeO-$	25.4	5.01
$MeCONH-$	10.1	0.99
$Me-$	13.6	3.37
$H-$	3.78	9.14
$Cl-$	17.7	3.72
$MeCO_2-$	4.87	1.01
$NC-$	4.36	0.32
O_2N-	4.49	0.19

LITERATURE REFERENCES

1. For reviews on singlet oxygen, see: (a) C.S. Foote, *Acc. Chem. Res., 1,* 104 (1968). (b) R.W. Denny and A. Nickon, *Organic reactions, 20,* 133 (1973). (c) "Singlet Molecular Oxygen," A.P. Schaap, ed., Dowden, Hutchinson, and Ross, Inc., Stroudsburg, PA, 1976. (d) "Singlet Oxygen," H.H. Wasserman and R.W. Murray, eds., Academic Press, New York, 2979. (e) A.A. Frimer, *Chem.Rev., 79,* 359 (1979).

2. (a) J. Eriksen, C.S. Foote, and T.L. Parker, *J. Am. Chem. Soc., 99,* 6455 (1977). (b) R.K. Haynes, *Aust. J. Chem., 31,* 121 (1978). (c) K.A. Brown-Wensley, S.L. Mattes and S. Farid, *J. Am. Chem. Soc., 100,* 4162 (1978). (d) I. Saito, K. Tamoto, and T. Matsuura, *Tetrahedron Lett.,* 2889 (1979). (e) W. Ando, T. Nagashima, K. Saito, and S. Kohnoto, *J. Chem. Soc., Chem. Commun., 154* (1979). (f) S.L. Mattes and S.Farid, *Ibid.,* 126 (1980). (g) J.Eriksen and C.S. Foote, *J. Am. Chem. Soc., 102,* 6083 (1980). (h) S.L. Mattes and S. Farid, *Ibid., 104,* 1454 (1982). (i) W. Ando, Y. Kabe, and T. Takata, *Ibid., 104,* 7314 (1982).

3. D. Rehm and A. Weller, *Isr. J. Chem., 8,* 259 (1970).

4. J. Eriksen and C.S. Foote, *J. Phys. Chem., 82,* 2659 (1978).

5. R.W. Ware, J.D. Holmes, and D.R. Arnold, *J. Am. Chem. Soc., 96,* 7861 (1978).

6. A.P. Schaap, K.A. Zaklika, B. Kaskar, and L. W.-M. Fung, *J. Am. Chem. Soc., 102,* 389 (1980).

7. Foote has reported the observation of radical-ion intermediates by laser flash techniques: L.T. Spada and C.S. Foote, *J. Am. Chem. Soc., 102,* 391 (1980).

8. E. Brunner and F. Dorr, *Ber. Bunsenges, Phys. Chem., 68,* 468 (1964).

9. A.P. Schaap, IX IUPAC Symposium on Photochemistry, Pau, France, July 26, 1982, Abstr. ST 15.

10. A.P. Schaap, L. Lopez, and S.D. Gagnon, *J. Am. Chem. Soc., 105,* 663 (1983).

11. A.P. Schaap, S. Siddiqui, S.D. Gagnon, and L. Lopez, *J. Am. Chem. Soc., 105,* 5149 (1983).

12. A.P. Schaap, S. Siddiqui, P. Balakrishnan, L. Lopez, and S.D. Gagnon, *Isr. J. Chem., 23,* 415 (1983).

13. A.P. Schaap, S. Siddiqui, G. Prasad, E. Palomino, and L. Lopez, *J. Photochem., 25,* 167 (1984).

14. A. Albini and D.R. Arnold, *Can. J. Chem., 56,* 2985 (1978).

15. (a) S, Futamura, S. Kusunose, H. Ohta, and Y. Kamiya, *J. Chem. Soc., Chem. Comm.,* 1223 (1982). (b) same authors, *J. Chem. Soc., Perkin I,* 15 (1984).

16. M. D. Sandison, Ph.D. Dissertation., Wayne State University, 1986.

17. R. Criegee and H. Korber, *Chem. Ber., 104,* 1807 (1971).

18. H.G. Heller and J.R. Langan, *J. Chem. Soc., Perkins I,* 341 (1981).

19. S.F. Nelsen, D.L. Kapp, R. Akaba, and D.H. Evans, *J. Am. Chem. Soc., 108,* 6863 (1986) and references therein.

20. E.L. Clennan, W. Simmons and C.W. Almgren, *J. Am. Chem. Soc., 103,* 2098 (1981).

21. Y. Kabe, T. Takata, K Ueno, and W. Ando, *J. Am. Chem. Soc., 106,* 8174 (1984).

22. (a) A.P. Schaap, R.S. Handley, and B.P. Giri, *Tetrahedron Lett.,* 935 (1987). (b) A. P. Schaap, T.S. Chen, R.S. Handley, R. DeSilva, and B.P. Giri, *Tetrahedron Lett.,* 1155 (1987). (c) A.P. Schaap, M.D. Sandison, and R.S. Handley, *Tetrahedron Lett.,* 1159 (1987).

23. R. Curci, L. Lopez, L. Troisi, S.M.K. Rashid, and A.P. Schaap, *Tetrahedron Lett.,* 5319 (1987).

24. R. Curci, L. Lopez, L. Troisi, S.M.K. Rashid, and A. Paul Schaap, *Tetrahedron Lett.,* in press.

25. I. Yamazaki in *Free Radicals in Biology,* W. Pryor ed., Vol. 3, pp. 183-218, Academic Press, NY, 1977.

26. (a) S. Kobayashi, M. Nakano, T. Goto, T. Kimura, and A.Paul Schaap, *Biochem. Biophys. Res. Comm., 135,* 166 (1986). (b) S. Kobashi, M. Nakano, T. Kimura, and A. Paul Schaap, *Biochem., 26,* 5019 (1987).